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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,740	08/25/2003	Douglas J. Dellinger	10990812-4	4681

22878 7590 09/28/2005

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EXAMINER

RILEY, JEZIA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 09/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/648,740

Applicant(s)

DELLINGER ET AL.

Examiner

Jezia Riley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5,9-11,18-26,29 and 30 is/are rejected.
- 7) ☒ Claim(s) 6-8,12-17,27 and 28 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8/25/03</u> . | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION***Double Patenting***

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 9-11, 29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-9, 13, 14, 22 of U.S. Patent No. 6,222,030. Although the conflicting claims are not identical, they are not patentably distinct from each other because both are claiming a method for synthesizing oligonucleotides comprising condensing support-bound monomer with a nucleoside having a carbonate protected hydroxyl group and oxidizing the phosphate trimer to give a phosphotriester using peroxide.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-3, 5, 18-26, 29, are rejected under 35 U.S.C. 102(e) as being anticipated by Pirrung et al. (5,908,926).

Pirrung et al discloses phosphoramidite oligonucleotide synthesis conducted on a solid support. 3'DMB carbonate is used to initiate synthesis. A second nucleotide is added as a 3' carbonate 5'phosphoramidite and coupling is effected. The resulting phosphite triester is then oxidized to phosphotriester (col.4-10). Col. 4 discloses that a nitrobenzyl carbonate can be used. The solvents used are benzene/pyridine (col 7), which is viewed as the mild pH of instant claim 2.

In column 6 it is described: Synthesis (5' to 3') using protected species (a), (b) and (c) can be carried out as follows. A 3'-DMB carbonate (a) is linked through a suitable linker to a support. The support is then irradiated at a wavelength in excess of 300 nm to free the 3' hydroxyl of the support-bound nucleoside (which is viewed as the free hydroxyl group on a support-bound nucleoside monomer of instant claim1). A second nucleotide is added as a 3' DMB carbonate-5'-phosphoramidite (b) (which is viewed as the nucleoside monomer having a protected group of step (a) in instant claim 1) and tetrazole-mediated coupling is effected. The resulting phosphite triester is oxidized using t-butylhydroperoxide, which is viewed as having the effect nucleophile of instant claim 1 as defined in applicants own specification page 1: " More particularly, the

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invention relates to an improved method for synthesizing oligonucleotides wherein carbonates are used as hydroxyl-protecting groups and "alpha-effect" nucleophiles such as peroxides are used in the deprotection thereof." Therefore t-butylhydroperoxide is viewed as having such effect.

Then unreacted 3' ends are capped, for example, using acetic anhydride/pyridine. Further irradiation results in the presentation of a new 3' end for the next coupling. The process of irradiation, coupling, capping and oxidation is repeated to provide the penultimate sequence.

Nucleic acid synthesis on a solid support requires: a chemistry for linking the growing chain to the support; a chemistry for effecting internucleotide linkage, including bond formation; and a chemistry for protecting functional groups on the heterocyclic bases. While these chemistries are described herein with reference to DNA synthesis, the approaches used are also applicable to RNA synthesis, with the addition of a protecting group for the 2' hydroxyl of ribose. Amino groups, where present on the bases, are protected by groups that can be removed without damaging the DNA backbone or the attachment to the support.(col.4-5).

Col. 10 shows that the phosphorous moiety can comprises an electron-withdrawing substituted phenyl.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

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said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-3, 5, 18-26, 29, 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pirrung et al. (US5,908,926) in view of Ravikumar (US5,705,621).

Pirrung et al. is discussed above.

However Pirrung do not show cleavage the synthesized oligo from the solid support.

Ravikumar discloses methods for the preparation of oligomeric compounds having phosphite, phosphodiester, phosphorothioate, or phosphorodithioate linkages, and to intermediates useful in their preparation, on solid support. Further it is disclosed that the completed oligomer is then cleaved from the solid support.

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Therefore it would have been obvious at the time the invention was made to synthesize oligonucleotide on solid support as taught by Pirrung and then cleave the oligonucleotides from the solid support as shown by Ravikumar. It is well known in the art to synthesize oligonucleotide on solid support and cleave it after the synthesis is complete. The motivation is that it produces oligonucleotides and their analogs, which are widely used as research reagents. They are useful for understanding the function of many other biological molecules as well as in the preparation of other biological molecules. For example, the use of oligonucleotides and their analogs as primers in PCR reactions has given rise to an expanding commercial industry. PCR has become a mainstay of commercial and research laboratories, and applications of PCR have multiplied. For example, PCR technology now finds use in the fields of forensics, paleontology, evolutionary studies and genetic counseling. Commercialization has led to the development of kits, which assist non-molecular biology-trained personnel in applying PCR. Oligonucleotides and their analogs, both natural and synthetic, are employed as primers in such PCR technology. (Ravikumar col. 2).

6. Claims 6-8, 12-17, 27, and 28 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


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7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Monday, September 26, 2005


JEZIA RILEY
PRIMARY EXAMINER